REMARKS

Reconsideration and reexamination of the present application are respectfully requested in light of the foregoing amendments and following remarks.

The amendments are made without prejudice or disclaimer of the canceled subject matter. Applicants reserve the right to file a continuing or divisional application on any subject matter canceled by way of amendment.

1. Status of the Claims

Claims 1, 4-7, and 23-24 are pending in the application. Claim 23 stands withdrawn for the reasons indicated in the Office Action, page 2. Claims 1, 4-7, and 24 are rejected. By entry of the amendment, claims 1, 4, and 5 are canceled, and new claims 25-30 are added.

Applicants note that claim 23 as amended is eligible for rejoinder upon an indication of allowance of claim 25, as a method of using the product of claim 25. *See In re Ochiai*, 71 F.3d 1565, 37 U.S.P.Q.2d 1127 (Fed. Cir. 1995); *In re Brouwer*, 77 F.3d 422, 37 U.S.P.Q.2d 1663 (Fed. Cir. 1996); Manual of Patent Examining Procedure, 8th ed., revised August 2006 (MPEP), § 706.02(n).

2. Support for the Amendments

The amendments are supported throughout the Specification and do not add new matter. Specifically, amended claims 6 and 23 and new claim 30 recite a pharmaceutical composition or a pharmaceutical acceptable carrier, which is supported in the Specification at page 15, line 13, *et seq.*, for example.

New claim 25 is supported throughout the Specification. A fragment of an N-acetylglucosaminyltransferase V (GnT-V) is supported throughout the specification, such as at page 41, line 24, *et seq.* (removing the transmembrane portion), or Example 5 (various amino terminal deletions). Support for GnT-V fragment up to 50 amino acids in length is found at page 14, lines 3-7, for example.

Support specifically for a basic amino acid cluster region comprising the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, is found at page 13, line 29, through page 14, line 7; page 15, lines 3-10; and the Sequence Listing, for example. Support for the phrase "wherein the number of amino acids modified by addition, removal, or substitution in the

variant is up to 10% of the number of amino acids in the basic amino acid cluster region" is supported, for example, at page 14, line 13, through page 15, line 12, particularly page 15, lines 3-10. Support for the phrase "wherein the addition, removal, or substitution is conducted on amino acids other than basic amino acids" is found, for example, at page 15, lines 10-12 of the Specification. Support for a fragment comprising a basic amino acid cluster region having neovascularization activity is found throughout the Specification, including claim 1.

Support for new claim 26 is also found at page 15, lines 10-12 of the Specification, for example. Support for new claim 27 is found in originally filed claim 4, for example. Support for new claim 28 is found at page 44, lines 15-17, of the Specification, for example, which discloses that the polypeptide of SEQ ID NO: 11 is sufficient for neovascularization activity. Support for new claim 29 is found at page 14, lines 13-15, of the Specification, for example. Finally, support for clam 30 is found at page 35, lines 18-28, for example.

3. Rejections under 35 U.S.C. § 112, Second Paragraph

3.1 Claim 6

Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office apparently alleges that it is unclear whether the "neovascularization accelerator" is the recited peptide or another component in the claimed neovascularization accelerator. Office Action, pages 3-4. Applicants traverse the rejection as it applies to the amended claim. As presently recited, claim 6 depends of claim 25. Claim 25 recites that the polypeptide possesses neovascularization activity, and thus is the component of the composition of claim 6 that accelerates neovascularization. The rejection accordingly may be withdrawn.

3.2 Claims 1 and 4-5

Claims 1 and 4-5 are rejected, because the phrase "an amino acid sequence of SEQ ID NO: 11" is allegedly confusing. Office Action, page 4. The phrase in question does not appear in the present claims, and the rejection accordingly is moot.

3.3 Claims 1 and 4-7

Claims 1 and 4-7 are newly rejected because "the recitation of 'neovascularization' in the context of the action of said peptide or polypeptide . . . is confusing." Office Action, page 4. While the Office admits that "'neovascularization' is clear," it is allegedly unclear "what is the specific role of said peptide or protein without having any specific activity or function rather having a neovascularization action." Applicants traverse the rejection as it applies to amended claims 6 and 7.

The grounds for the rejection are not clearly stated. The Office apparently alleges that the claims are directed to a polypeptide having an activity other than neovascularization activity. If the Office intends to allege something else, the Office is urged to provide authority for the alleged requirement and make the next Office Action non-final, should there be a necessity for another Office Action.

Claims are construed during prosecution as the skilled artisan would understand the claims, when read in light of the Specification. *In re Morris*, 127 F.3d 1048, 1054, 44 U.S.P.Q.2d 1023, 1027 (Fed. Cir. 1997). Present claims 6 and 7 depend on claim 25, which recite a polypeptide fragment possessing neovacularization activity. The Office has presented no evidence or reasoning why the skilled artisan would be confused by the recitation of a peptide possessing a specific biological activity. The Office particularly has presented no evidence or reasoning why the skilled artisan would be confused by the recitation of "wound healing agent" in claim 7 that comprises the polypeptide fragment possessing neovascularization activity recited in claim 25. The present claims thus are clear, particularly in view of the Office's admission that the term "neovascularization" is clear absent a grounded argument that supports a *prima facie* case of indefiniteness. The rejection accordingly should be withdrawn.

3.4 Claim 5

The Office rejects claim 5, alleging that "a new peptide of 'SEQ ID NO: 7' " is unclear. The rejection is moot in view of the cancellation of claim 5.

For the Office's convenience, the relationship between SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 11 is depicted below:

MALFTPWKLSSQKLGFFLVTFGFIWGMMLLHFTIQQRTQPESSSMLREQILDLSKRYI
KALAEENRNVVDGPYAGVMTAYDLKKTLAVLLDNILQRIGKLESKVDNLVVNGTG
TNSTNSTTAVPSLVALEKINVADIINGAQEKCVLPPMDGYPHCEGKIKWMKDMWRS
DPCYADYGVDGSTCSFFIYLSEVENWCPHLPWRAKNPYEEADHNSLAEIRTDFNILY
SMMKKHEEFRWMRLRIRRMADAWIQAIKSLAEKQNLEKRKRKKVLVHLGLLTKES
GFKIAETAFSGGPLGELVQWSDLITSLYLLGHDIRISASLAELKEIMKKVVGNRSGCPT
VGDRIVELIYIDIVGLAQFKKTLGPSWVHYQCMLRVLDSFGTEPEFNHANYAQSKGH
KTPWGKWNLNPQQFYTMFPHTPDNSFLGFVVEQHLNSSDIHHINEIKRQNQSLVYGK
VDSFWKNKKIYLDIIHTYMEVHATVYGSSTKNIPSYVKNHGILSGRDLQFLLRETKLF
VGLGFPYEGPAPLEAIANGCAFLNPKFNPPKSSKNTDFFIGKPTLRELTSQHPYAEVFI
GRPHVWTVDLNNQEEVEDAVKAILNQKIEPYMPYEFTCEGMLQRINAFIEKQDFCHG
QVMWPPLSALQVKLAEPG [SEQ ID NO: 6]

Underlined sequence = SEQ ID NO: 11
Highlighted sequence = SEQ ID NO: 7

3.5 Claim 24

The Office alleges that the term "preventing" in claim 24 is indefinite. Office Action, page 5. The term is not present in the amended claims, and the rejection thus is moot.

4. Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1, 4-7, and 24 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office asserts that the claims purportedly encompass a number of species in the genus that are not adequately described, because allegedly the specification only teaches the structure of a single representative species of such proteins. Office Action, pages 5-7. Applicants traverse the rejection as it applies to the amended claims.

The Office requires description of a representative number of species to define the claimed genus of species, based on an alleged substantial variation in structure within the claimed genus of polypeptides. Office Action, page 7. The written description requirement, however, may be satisfied for proteins and nucleic acids, where the specification provides "sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Monsanto Co. v. Scruggs*, 459 F.3d 1328, 79 U.S.P.Q.2d 1813, 1818 (Fed. Cir. 2006) (quoting *Enzo Biochem Inc., v. Gen-Probe Inc.*, 323 F.3d 956, 964, 63 U.S.P.Q.2d 1609, 1618 (Fed. Cir. 2002)).

In the present case, the claimed invention is directed to a polypeptide fragment of an N-acetylglucosaminyltransferase V (GnT-V), comprising a basic amino acid cluster region, (1) wherein the basic amino acid cluster region comprises the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, (2) wherein the polypeptide fragment or variant thereof possesses neovascularization activity, (3) wherein the number of amino acids modified by addition, removal, or substitution in the variant is up to 10% of the number of amino acids in the basic amino acid cluster region, and (4) wherein the addition, removal, or substitution is conducted on amino acids other than basic amino acids.

The Office alleges that the basic amino acid cluster region having the amino acid sequence of SEQ ID NO: 11 does not provide sufficient structure for the claimed polypeptides to possesses neovascularization activity. Office Action, page 6. To the contrary, the polypeptide of SEQ ID NO: 11 ***by itself*** possesses neovascularization activity. *See, e.g.*, Specification, page 44, line 15, *et seq.* Further, GnT-V fragments comprising SEQ ID NO: 11 also possess neovascularization activity, including Gnt-VΔ73 (page 41, line 24, *et seq.*; page 46, lines 3 – 21); Gnt-VΔ188 (page 42, line 18, *et seq.*; page 46, line 23 – page 47, line 6); and Gnt-VΔ233 (page 42, line 18, *et seq.*; page 46, line 23 – page 47, line 6).

All the polypeptide fragments encompassed by the claims comprise the amino acid sequence of SEQ ID NO: 7, which encompasses SEQ ID NO: 11. Because the peptide of SEQ ID NO: 11 possess neovascularization activity, ***all*** the polypeptide fragments encompassed by the claims likewise would be expected to possess neovascularization activity. The claims are adequately described, because the Specification describes functional characteristics of the claimed compounds, coupled with a disclosed correlation between function and structure. *See Monsanto*, 79 U.S.P.Q.2d at 1818; *Enzo*, 63 U.S.P.Q.2d at 1618.

The claimed variants have amino acid modifications conducted on amino acids other than basic amino acids. The claimed variants therefore possess the sequence KRKRKK (SEQ ID NO: 11), which is sufficient for neovascularization activity, for the reasons set forth above. It follows that all the claimed variants likewise would be expected to possess neovascularization activity. Thus, for the same reason as the polypeptide fragments, the Specification adequately describes the recited variants. *See Monsanto*, 79 U.S.P.Q.2d at 1818; *Enzo*, 63 U.S.P.Q.2d at 1618. Accordingly, the rejection should be withdrawn.

5. Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1, 4-7, and 24 are rejected, because the specification "while being enabling for a protein having neovascularization accelerating activity encoded by SEQ ID NO: 6 from human with identifying properties such as converting of N-acetylglucosamine into α-6-D-mannoside using UDP-N-acetylglucosamine as substrate, specificity as defined in claim 2, optimum pH...," the specification allegedly "does not reasonably provide enablement for any peptide or any protein having neovascularization activity from any source or any protein sequence with modification of one or more amino acids or any peptide sequence with modification of one or more amino acids to SEQ ID NO: 7." Applicants traverse the rejection to the extent it applies to the amended claims as amended.

Applicants note for the record that the presently claimed polypeptide possesses neovascularization activity without necessarily possessing glycosyltransferase activity. *See, e.g.*, specification, page 43, lines 20-24.

All the claimed polypeptide fragments comprise a basic amino acid cluster region having the amino acid sequence of SEQ ID NO: 11, which is part of SEQ ID NO: 7. Applicants demonstrate that SEQ ID NO: 11, KRKRKK, is ***sufficient*** for the polypeptide fragment to possess neovascularization activity. *See, e.g.*, Specification, page 45, lines 22-27 ("the KRKRKK peptide accelerated growth of HUVEC at the same degree as GnT-VΔ73. . . . These results suggest that a basic amino acid cluster region of GnT-V is sufficient for an HUVEC growth accelerating activity. . . ."); *see also* Specification, pages 46-48, FIGURES 3, 4, 5, and 6, etc. The Specification provides further evidence that polypeptide fragments of SEQ ID NO: 6 that comprise SEQ ID NO: 11 possess neovascularization activity: Gnt-VΔ73 (page 41, line 24, *et seq.*; page 46, lines 3 – 21); Gnt-VΔ188 (page 42, line 18, *et seq.*; page 46, line 23 – page 47, line 6); and Gnt-VΔ233 (page 42, line 18, *et seq.*; page 46, line 23 – page 47, line 6).

The Office provides no evidence that members of the genus would not have the stated activity. Further, the Office advances no evidence that merely adding, deleting, or substituting amino acids to a polypeptide would require more than the exercise of routine skill. The present claims are not drawn to an "extremely large number of proteins or peptides including mutants and variants having neovascularization activity." Office Action, page 9. The enabling disclosure instead in commensurate with the scope of the claims, because all the

recited polypeptides comprise SEQ ID NO: 7, which is sufficient for neovascularization activity. Further, all the recited variants are modified in amino acids other than basic amino acids, meaning that they, too possess the sequence KRKRKK, which is sufficient for neovascularization activity. Contrary to the allegations in the Office Action (pages 9-10), the specification establishes which regions of the claimed polypeptides may be modified without losing neovascularization activity (i.e., thus outside the region KRKRKK), and provides sufficient guidance and direction to the skilled artisan to make polypeptide fragments and variants thereof that possess neovascularization activity. The presently claimed polypeptide fragments thus would not require undue experimentation to make and use, and the rejection should be withdrawn.

6. Rejections under 35 U.S.C. § 102

6.1 Taniguchi

Claim 5 is rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,834,284 ("Taniguchi"). Applicants traverse the rejection as it applies to the amended claims.

Taniguchi discloses a full length GnT-V protein having glycosyltransferase activity at col. 1, lines 46-63. Taniguchi, however, does not disclose at least a polypeptide fragment of an N-acetylglucosaminyltransferase V (GnT-V) comprising a basic cluster region that comprises the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, as presently recited. Because Taniguchi does not teach each and every element of the claimed invention, the rejection should be withdrawn. *See Verdegaal Bros. v. Union Oil Co. Cal.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *see also* MPEP § 2131.

6.2 Nakahara

Claims 1, 4-7, and 24 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 6,191,113 B1 ("Nakahara"). Applicants traverse the rejection as it applies to the amended claims.

Nakahara discloses at col. 3, lines 42-52, a peptide comprising a peptide A that contains abundant basic amino acid residues, and a peptide B that comprises at least two consecutive, hydrophobic amino acids. The disclosed peptides A and B are linked via several

amino acid residues. The peptide disclosed in Nakahara contains a sequence identical to SEQ ID NO: 11.

Nakahara does not teach at least a polypeptide fragment of an N-acetylglucos-aminyltransferase V (GnT-V) comprising a basic cluster region that comprises the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, as presently recited. Because Nakahara does not teach each and every element of the claimed invention, the rejection should be withdrawn. *See Verdegaal*, 814 F.2d at 631; *see also* MPEP § 2131.

6.3 Selwood

Claims 1, 4-7, and 24 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 02/34767 A1 ("Selwood"). Selwood is not available as prior art, based on Applicants' claim to priority under 35 U.S.C. § 119(a).

Further, Selwood teaches a VEGF fragment that inhibits angiogenesis. Although the disclosed VEGF fragment (SEQ ID NO: 10) contains a sequence identical to SEQ ID NO: 11, the disclosed sequence does not comprise a basic cluster region that comprises the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, as presently recited. Because Selwood is unavailable as prior art and does not teach each and every element of the claimed invention, the rejection should be withdrawn. *See Verdegaal*, 814 F.2d at 631; *see also* MPEP § 2131.

6.4 Tischer

Claims 1, 4-7, and 24 are rejected under 35 U.S.C. § 102 as allegedly anticipated by Tischer *et al.*, *J. Biol. Chem.* 266: 11947-54 (1991) ("Tischer"). Applicants traverse the rejection as it applies to the amended claims.

Tischer discloses a VEGF peptide that contains a sequence identical to SEQ ID NO: 11. Tischer does not teach a polypeptide fragment of an N-acetylglucosaminyltransferase V (GnT-V) according to the present claims. In particular, the disclosed sequence of Tischer does not comprise a basic cluster region that comprises the amino acid sequence of SEQ ID NO: 7 and up to 50 contiguous amino acids encoded by the sequence shown in SEQ ID NO: 6, or a variant thereof, as presently recited. Because Tischer does not teach each and every

element of the claimed invention, the rejection should be withdrawn. *See Verdegaal*, 814 F.2d at 631; *see also* MPEP § 2131.

CONCLUSION

Should the Examiner have any questions or comments regarding Applicants' amendments or response, he is asked to contact Applicants' undersigned representative at the telephone number below. Please direct all correspondence to the below-listed address.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is respectfully requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: October 31, 2007

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